NEW DIRECTIONS IN EYE BANKING

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INTRODUCTION

THE VAST POTENTIAL FOR THE USE OF CORNEAL DONOR MATERIAL AS WELL AS advancements in microsurgical techniques, instrumentation, and suture material have all played a role in the development of eye banks. Their resultant establishment has changed keratoplasty from a rare, experimental procedure into an operation frequently used in the treatment of corneal disease. Between 1950 and 1970, because of increasing interest by ophthalmologists in performing keratoplasties, there was a rapid proliferation of eye banks not only in academic centers but throughout the United States.

As we enter a new decade with the need of eye banks firmly established, this field has assumed a new sophistication and direction. The purpose of this paper is to examine the present-day attention of eye banking to the important aspects of funding, sources of donor tissue, intermediate-term preservation techniques, and quality control, as well as to illustrate the ability to retrieve scientific data on various aspects of keratoplasty through computer analysis.

MILESTONES IN THE HISTORY OF KERATOPLASTY

The development of keratoplasty is an exciting chapter in the history of ophthalmology, written about by many in great detail[1,2] (Table I). De Quengsy,[3] in 1789, first suggested the replacement of excised opaque cornea with a convex disc of clear glass sewn onto the recipient cornea. Later, Darwin speculated that corneal scars might be excised "by a kind of trephine" and perhaps "heal with a transparent scar. . . . This experiment is worth trying. . . . I wish strongly to recommend [it] to some ingenious surgeon or oculist."[4]

Although Himly apparently first suggested actual keratoplasty in 1813, his student Reisinger,[5] experimenting on chickens and rabbits in 1824, was the first to perform penetrating keratoplasties. In 1837 Bigger reported on

TABLE I: MILESTONES IN HISTORY OF KERATOPLASTY

1824	Reisinger[5]	First experimental PK* in animals
1837	Bigger[6]	PK on pet gazelle, homologous donor
1838	Kissam[7]	First PK in man, heterologous donor
1872	Power[8]	PKs on humans, heterologous donors
1878	Sellerbeck[9]	First LK† in man, homologous donor
1886	Von Hippel[10]	First partial success, LK in man, heterologous donor
1894	Fuchs[11]	LK in 30 patients, heterologous and homologous donors
1900	Salzer[12]	Importance of homologous donor tissue
1906	Zirm[13]	First successful PK in man, homologous donor
1911	Magitot[14]	Preservation in human donor tissue
1930	Elschnig[18]	PK in 174 patients, 73% success in IK‡
1935	Filatov[19]	PK in 96 patients, use of cadaver donor tissue
1944	Paton[21]	Eye Bank for Sight Restoration, Inc
1974	McCarey, Kaufman[32]	Intermediate-term corneal preservation

*PK = Penetrating keratoplasty.
†LK = Lamellar keratoplasty.
‡IK = Interstitial keratitis.

the successful transplantation of a cornea from a dying gazelle into a blind pet gazelle's eye while he was a prisoner of a "Nomadie [sic] tribe of Arabs . . . in Egypt . . . 12 to 14 days' journey from Grand Cairo."[6] The upper cornea remained clear, and the animal gave unequivocal signs of vision ten days postoperatively. He suggested the use of pig cornea as potential donor material in human beings. Following Bigger's advice, Kissam[7] used the cornea of a 6-month-old pig to replace the staphylomatous cornea of a blind man. The cornea clouded within a month. Following the failure of this and other similar keratoplasties using heterologous donors, the interest in the operation in human beings decreased. Meanwhile, general anesthesia was introduced in 1846, and the principles of antisepsis were proclaimed by Lister in 1867. Both these advances set the stage for future successes. In 1872 Power[8] reported his experiments with keratoplasty, using heterologous and homologous donor tissue in animals and using rabbit cornea as donor tissue in human beings. He suggested that homoplastic donor material should be preferred because of the difference in structure and thickness between the human cornea and other species. Sellerbeck,[9] in 1878, was the first to do a lamellar keratoplasty in a human being using human donor tissue.

Von Hippel,[10] who had invented the circular trephine, popularized the lamellar keratoplasty technique in human beings, using heterologous donor tissue. In the first limited success in a human being in 1886, he performed a lamellar transplant on a young girl using a full-thickness rabbit cornea, and her vision improved from counting fingers to 20–200.

In 1894 Fuchs[11] reported on lamellar grafts in 30 patients. The donor material was from rabbits in 14, from enucleated pathologic human eyes in 11, from a dog in 1, and from stillborn infants in others. None of the grafts

remained perfectly clear, and the visual results were not encouraging. Six years later, Salzer[12] enumerated the differences between various types of donor tissue: autografts, homografts, and heterografts. He recognized autoplasty as the most favorable procedure but with few applications. He advocated the use of homologous donor material in patients, preferably from stillborn infants or embryos.

In 1906 Zirm[13] reported the first successful penetrating keratoplasty using human donor tissue, which was obtained from an 11-year-old boy whose eye was enucleated following a perforating injury. The recipient had sustained lye burns and the graft remained relatively clear for several years, at least, with a fair visual results.

In the next few years, Magitot,[14] an ophthalmologist in Paris, began the first research on the preservation of donor corneal tissue. He experimented on animals, preserving the whole eyes in serum from animals of the same species at 5 to 8 C, and reported "perfect preservation" of the tissues for from 12 to 14 days. In 1911 he performed a successful lamellar keratoplasty on a 14-year-old boy with a dense pseudopterygium from a previous lye burn. He had preserved the donor eye, enucleated for intractable glaucoma, for eight days in a solution of hemolyzed blood-serum taken from another person. The graft had remained clear for nearly a year when he reported the case a year later. He also emphasized the importance of homologous donor tissue to the success of keratoplasty. "I am, consequently, convinced that for the first time a successful transplantation has been made by the aid of corneal tissue preserved for several days in a state of vitality. I believe I have obtained as good a result as if I had made use of fresh material. . . . My method encourages the hope that this useful operation will soon be generally employed."[14] Thus, as he laid the foundation for eye banking and corneal preservation, Magitot predicted the widespread acceptance of keratoplasty that would take another 40 years to achieve.

Because of the high failure rate in penetrating keratoplasty, interest for the next 30 years was directed primarily to lamellar grafts. The disastrous consequences of infection were lessened, but the optical results were not as good. In the ensuing years there were scattered reports of successful total penetrating keratoplasties.[15-17] In 1930, however, Elschnig[18] reported on his large series of 174 penetrating keratoplasties from Prague. He used a trephine from 4.0 to 4.5 mm in diamater—hence the term "partial penetrating" as not encompassing the full width of the cornea. He reported a success rate of 22% of the 139 cases done for leukomas following burns or ulcerations. In the 26 cases done for leukomas from interstitial keratitis, however, his success rate was 73%.

During the same period Filatov,[19] of Odessa, USSR, was also pioneering in penetrating keratoplasty with the daring use of cadaver tissue for donor material. In 1935 he reported on 96 penetrating keratoplasties performed between 1923 and 1932. Although his overall success rate was low, in the 26 cases he operated on for leukomas in which some transparent corneal tissue remained, there were clear grafts in 54% (14). Cadaver eyes enucleated within a few hours after death, preserved at 4 to 6 C, and used between 20 to 56 hours after death were the donor tissue in 35 of the cases, He concluded "that the using of transplants from cadavers' eyes has a good prospect of success."[19] He called for a thorough study on the "methods of preservation of the material at a certain temperature and under aseptic conditions" and sought government assistance "to simplify the process of obtaining cadavers' eyes."[19] Modern eye banking, conceived by Filatov, was born in Odessa.

EYE BANK ORGANIZATIONS IN THE UNITED STATES

EYE BANK FOR SIGHT RESTORATION, INC

In late 1944 Townley Paton, MD, and John MacLean, MD, established an experimental "eye bank" at the New York Hospital.[20] In 1945 Dr Paton,[21] with the enthusiastic support of Mrs Aida Breckinridge, founded the Eye Bank for Sight Restoration, Inc. Thirty-two hospitals in the New York area were initially affiliated with the eye bank. By 1950 its supply of donor tissue had exceeded 1,200 eyes.[22] Because of the tremendous public interest in the keratoplasty operation itself and its often dramatic restoration of sight in certain types of blindness, there was a sudden surge of publicity that often exaggerated results without informing the public of the limitations inherent in patient selection.[23,24] By 1956 branch eye banks were operating in Boston, Philadelphia, Winston-Salem, New Orleans, Chicago, San Francisco, and Los Angeles.[25]

The primary aims of the Eye Bank for Sight Restoration, Inc, were to provide a supply of donor material to qualified surgeons, to support research in and teaching of the surgical techniques, to provide ocular tissue for experimental work, and to stimulate research in the causes of blindness, particularly from corneal disease or injury. These original goals have guided eye banks for the past 35 years.[21,25]

EYE BANK ASSOCIATION OF AMERICA

The American Academy of Ophthalmology and Otolaryngology formed a committee on eye banks in 1957 "to advise and aid eye banks to operate on

a firm medical basis, to give medical advice to eye bank medical directors, and to attempt standardization of some of the procedures concerned in the eye banks."[26]

In 1961, with the support of the Academy, the Eye Bank Association of America (EBAA) was formed, with 35 eye banks accepted as charter members. Its purpose was "to coordinate the activities of eye-banks, to stimulate the donation of eyes, to establish national legislation on eye donations, and to encourage and finance much needed research in the prevention and treatment of blinding eye disease."[27] As of 1978, there were 68 member eye banks.[28]

EYE BANK EMERGENCY NETWORK

The Eye Bank Emergency Network (NET) is a group of ham radio operators in major cities throughout the United States who on a volunteer basis daily provide a communication network for eye banks and corneal surgeons throughout the country. The NET was founded in December 1962 by Alson E. Braley, MD, then Chairman of the Department of Ophthalmology at the University of Iowa, and Professor Ted Hunter of the Department of Physics at the University. Both these men were ham radio operators who realized the tremendous contributions that were to be made by a nationwide ham radio system to aid in the location and utilization of available donor tissue. Within a year the network had grown to 60 operators in 47 cities throughout 26 states. As of August 1977, the radio network had facilitated the distribution of available donor tissue in 8,964 cases.[29]

THE MEDICAL EYE BANK

The Medical Eye Bank Inc (MEB) was established in Baltimore, Md in 1962. By 1967 a full-time director was hired and by 1980 the full-time staff had expanded to 12, with several parttime employees. The author became medical director in 1972. It was apparent at that time that eye banking in the United States had five main areas that needed attention:

1. Financial support was limited and derived almost entirely from the private sector.
2. Sources of donor tissue were undependable and precluded scheduled elective keratoplasty.
3. Clinical pathologic correlation of ocular disease could be furthered by eye bank support.
4. There was little standardization of techniques, and the importance of good quality control was not universally appreciated.

5. Follow-up information was needed to assess quality control and the key variables in corneal surgical procedures.

EYE BANK FUNDING

Eye banks in the United States are either totally independent organizations or they are operated under the aegis and with the logistic support of hospitals and university centers. Previously, both kinds have relied heavily on the private sector for financial support.

The Lions Club International, the American Legion, foundations, local United Fund drives, and individuals all annually contribute time and money toward the operation of eye banks. It was initially difficult to employ the sophisticated personnel necessary for an efficient, high-quality operation and still balance the budget. The EBAA had made it a part of its code of ethics that no donor tissue could "be bought or sold."[30] However, other tissue banks, notably kidney banks, were receiving third-party reimbursements to support their operation. By 1971, budgetary constraints were forcing the MEB to consider limiting its own supply of tissue to use within the state. Because of these factors the Medical Board approved unanimously the concept of billing third-party health insurance companies for the cost of processing donor eye tissue. Agreements were reached with the local Blue Cross and Medicare officials to accept reasonable fees billed through local hospitals for our services. Several years later similar arrangements were made in most of the other states where the MEB sent donor tissue. In 1979 the MEB, which previously had depended totally on fund raising and charity support, derived 75% of its operating budget from fees paid by third-party insurers for processing costs. This concept is now accepted by the EBAA, and most eye banks derive some support from processing fees.

Eye banking reached a sound financial footing and now can assume the higher costs that good quality control requires. Moreover, as pointed out by Cavanagh[31] in a nationwide survey of 50 eye banks, the cost-effectiveness (annual budget of an individual eye bank divided by the number of its donor eyes used for transplants) is far superior in the large eye banks that process a great amount of donor tissue than in the smaller, parttime operations.

MEDICAL EXAMINER'S LAW: NEW SOURCES OF DONOR MATERIAL

Good donor tissue still remains in short supply. Many corneal surgeons have lists of keratoplasty candidates waiting for good donor tissue. Conse-

quently, in most areas corneal surgical procedures cannot be electively scheduled but most be done whenever donor tissue becomes available.

The advent of intermediate-term preservation of donor tissue by the McCarey-Kaufman technique (MK medium) opened a new era in eye banking.[32,33] In 1974 the MEB became the first to adopt this technique for the preservation of corneas obtained from the usual hospital sources, at the specific request of the next of kin.

However, it was apparent that a constant supply of young donor tissue for preservation by this method would be available from the Medical Examiner's office, if appropriate legislation could be passed. In December 1974, the author composed the wording of a statute that was to be enacted by the state legislature in March 1975. (Appendix) The law was carefully written in order not to offend the public, the legislators, or the morticians' lobby. Its successful passage was a tribute to the intense efforts of the executive director of the MEB, interested ophthalmologists, the Medical Examiner himself, and many other persons.

This law, the first of its kind, allows donor corneal tissue with a rim of sclera to be removed immediately from the eyes of any Medical Examiner's case requiring autopsy, unless specifically forbidden by the next of kin. In effect, the law makes it unnecessary to consult the next of kin for permission; thus, most autopsied cases are potential donors.

This revolutionary law has provided the MEB with a constant source of good donor tissue, preserved in MK solution. In 1976 the average donor age of tissue from the Medical Examiner was 30 years compared with an average age of 56 years in donor tissue received from all other sources. By 1979, 79% of our donor tissue used for surgical procedures came from the Medical Examiner's office. Table II illustrates the growth of the MEB since 1964 and its increased use of the Medical Examiner's office as a source of good donor tissue. Corneal surgeons in our area can now schedule keratoplasties ahead of time and be reasonably assured of good donor tissue. Following this example, four or five other states have now passed similar laws, as has the Republic of South Africa. Each has experienced a great improvement in the supply of corneal donor tissue without public controversy.

However, quality control becomes more critical if an eye bank undertakes this sort of a program. The source of donor material must be carefully screened to avoid using donor tissue from persons with known or unsuspected diseases that might be contraindicated. Moreover, the increased handling of the tissue requires highly skilled employees. Today's eye bank technicians must be intelligent persons who are trained in sterile technique, surgically competent, and able to peruse medical records for perti-

nent facts. Obviously, the need for and use of this sophisticated personnel increase both the cost and complexity of operating an eye bank.

SPECIAL EYE DONOR PROGRAM FOR HISTOPATHOLOGIC STUDIES

The MEB has instituted a special program in collaboration with the Wilmer Eye Pathology Laboratory in which patients will their eyes for post mortem histopathologic study. All ophthalmologists in the area have been made aware of this program and have been provided with special donor cards and information for prospective donors. Patients with ocular conditions that warrant histopathologic study are urged to participate. Donor cards for these patients are specially filed at the MEB. This effort is an important responsibility of eye banks and will help to improve the clinical pathologic correlation in a number of ocular diseases in the future.

QUALITY CONTROL IN EYE BANKING

The importance of good donor tissue for the success of PK has been understood since the beginning of corneal surgery and was emphasized by Paton[21] with the founding of the Eye Bank for Sight Restoration, Inc. However, quality control of donor tissue in eye banking is a more recent concept. While it is generally agreed that the ultimate responsibility for donor tissue lies with the operating surgeon, that surgeon must depend heavily on the eye bank processing the donor tissue for good quality control within its own organization. There are five main reasons for this increased recognition of the importance of quality control in eye banking: (1) the increased frequency of reports in the literature and lay press concerning the transmission of corneal donor disease to recipients; (2) increased reports of endophthalmitis following penetrating keratoplasty; (3) the understanding of primary donor tissue failure and its relation to donor factors and hours of storage; (4) the recent use of intermediate-term corneal storage with MK solution: it has increased the handling of donor tissue by eye bank technicians and consequently caused a greater potential for contamination, mechanical damage to the donor tissue endothelium, or osmotic or chemical damage or both from the medium; and (5) the pressure from patients with their demands for near perfect results in the management of their health care by physicians.

TRANSMISSION OF DONOR DISEASE TO CORNEAL RECIPIENTS

There are nine reports in the literature concerning the transmission of donor disease to corneal recipients (Tables III & IV). Hata[34] reported the

TABLE II: DONOR TISSUE: SOURCES AND UTILIZATION

	Hospital Sources			Medical Examiner's Office			Total	
Yr	No. collected	Used for surgery	% used	No. collected	Used for surgery	% used	Collected	Used
1964	249	127	51	. . .	. . .	. . .	249	127
1967	390	215	55	. . .	. . .	. . .	390	215
1969	2,244	913	41	. . .	. . .	. . .	2,244	913
1971	2,078	704	34	. . .	. . .	. . .	2,078	704
1974	1,725	891	50	. . .	. . .	. . .	1,725	891
1976	1,275	542	43	1,074	634	59	2,349	1,176
1978	1,528	177	12	1,317	909	69	2,845	1,086
1979	1,582	318	20	1,713	1,379	81	3,295	1,697

first in the Japanese literature in 1939. The donor eye had a retinoblastoma. It is not clear whether the donor eye was being enucleated for retinoblastoma or whether the patient died with a retinoblastoma. However, within 1½ years, iritis and secondary glaucoma developed in the recipient eye. Subsequent enucleation showed a retinoblastoma of the anterior segment.

DeVoe,[35] in the Gifford Lecture in 1974, reported the case of a 55-year-old woman with Fuchs' dystrophy on whom he had done a corneal transplant in 1971. The donor had died with the then obscure Creutzfeldt-Jakob disease. The graft did well with the vision improving to 20/25 acuity. However, in 18 months a progressive neurologic disorder developed, and the patient died 27 months following penetrating keratoplasty with the same Creutzfeldt-Jakob disease.[36]

In 1976, LeFrancois and Baum[37] reported on an 80-year-old woman who received a corneal transplant for aphakic bullous keratopathy. Within 24 hours, an endophthalmitis developed that was refractory to antibiotic therapy. *Flavobacterium meningosepticum* was isolated from the infected eye by anterior chamber paracentesis, from the residual donor corneal-scleral rim, and from culture medium in which the donor tissue had been stored. Cultures were done on the stock bottle of residual MK medium, on the neomycin-gramicidin-polymyxin B (Neosporin) solution from the same bottle used to prepare the donor eye, and on the jars that originally contained the whole donor eyes. All these cultures were negative. As *Flavobacterium* is a common contaminant found in soil and water, one cannot be certain whether this was a result of initial contamination of the donor eye itself or the preservation technique.

In 1977, Shaw and Aquavella[38] reported on the corneas and kidneys that were used from a 12-year-old boy with a severe head injury who had been on cardiovascular life support for 26 hours. He initially became febrile with a temperature of 39.3 C (102.8 F). He had received antipyretics and hypothermia in an attempt to lower his body temperature. After two consecutive flat electroencephalograms, 36 hours after admission, both the eyes and kidneys were donated for transplantation by the family. Both kidney recipients died suspiciously of "myocardial infarction" within 48 hours. Pneumococcal endophthalmitis developed in both corneal recipients with subsequent loss of their eyes. Post mortem examination of the donor showed a bronchial pneumonia although "no active organisms were cultured" from the donor.

Beyt and Waltman[39] reported on a 25-year-old donor with polymositis who had been on long-term corticosteroid and immunosuppressive therapy and who died after a 28-day downhill course with progressive pneumo-

TABLE III: TRANSMISSION OF DONOR DISEASE: CASE REPORTS

Case no.	Date	Authors	Donor age, sex	Donor disease	Donor actual cause of death	Preservation	Recipient age, sex
1	1939	Hata[34]	4, . . .	Retinoblastoma		Moist chamber	. . .
2	1974	DeVoe[35]	55, M	Progressive neurologic disease	Creutzfeldt-Jakob	Moist chamber	55, F
3	1976	LeFrancois and Baum[37]	57, M	Myocardial infarction	Myocardial infarction	Enucleated in 3 hr MK for 19 hr	80, F
4	1977	Shaw and Aquavella[38]	12, M	Head trauma, fever Hypothermia and cardiovascular support 26 hours	Bronchial pneumonia	Moist chamber 12 hr	60, M
5						Moist chamber 14 hr	34, F
6	1978	Beyt and Waltman[39]	25, F	Polymyositis, corticosteroid and immunosuppressive therapy	Disseminated cryptococcus	MK for 48 hr	83, F
7	1979	Khodadoust and Franklin[40]	45, M	Hodgkin's disease, peritonitis	Probable septicemia	Moist chamber 2 hr	26, M
8						Moist chamber 6 hr	42, M
9	1979	Houff et al[41]	39, M	Progressive neurologic disease (22 days)	Rabies	Moist chamber for several hr	37, F

TABLE IV: TRANSMISSION OF DONOR DISEASE: CASE REPORTS

Case no.	Reason for PK*	Disease in recipient	Onset after PK	End result	Linkage
1	Corneal dystrophy	Hypopyon, glaucoma	1½ yr	Enucleation	Retinoblastoma
2	Fuchs' dystrophy	Progressive neurologic disease	18 mo	Death, 27 mo after PK	Creutzfeldt-Jakob
3	Aphakic bullous	Endophthalmitis	24 hr	Phthisis	*Flavobacterium meningosepticum* cultured from anterior chamber and residual corneal rim, not from original stock of TC 199
4	Leukoma, failed PK	Endophthalmitis	24 hr	Enucleation	Pneumococcus, OU Both kidney recipients dead from "myocardial infarction" in 48 hours
5	Fuchs', aphakic bullous	Endophthalmitis	48 hr	Phthisis	
6	Aphakic bullous	Yellow-white mass in anterior chamber	2 mo	LP, cloudy cornea	Cryptococcus
7	Keratoconus	Endophthalmitis	24 hr	Regraft, phthisis	*Pseudomonas aeroginosa*, OU
8	Herpetic leukoma	Endophthalmitis	10 hr	Regraft, 20/30	
9	Keratoconus	Progressive neurologic disease	25 days	Death, 50 days after PK	Rabies

*PK = Penetrating keratoplasty.

nia and respiratory failure. Blood cultures for bacteria were negative. Subsequent autopsy revealed disseminated cryptococcosis with lung and brain abscesses. Two months after keratoplasty, a 3-mm yellow-white mass developed in the anterior chamber in one recipient eye. A diagnosis of cryptococcal endophthalmitis was made on the basis of finding typical organisms in aqueous obtained by paracentesis as well as subsequent positive aqueous cultures. The eye was lost despite topical and systemic amphotericin B and flucytosine therapy. The recipient of the fellow donor cornea continues to do well six months after keratoplasty.

Khodadoust and Franklin[40] recently published two cases of *Pseudomonas* endophthalmitis following keratoplasty in Iran, using tissue from a donor with Hodgkin's disease who died with acute peritonitis and a probable septicemia. In both recipients a fulminating endophthalmitis developed within 24 hours from *Pseudomonas aeruginosa*. Despite vigorous antibiotic therapy and regrafting, one recipient eye was lost. The other recipient eye did well with antibiotics and regrafting. It is strongly suspected that the donor had an unrecognized *Pseudomonas* septicemia.

Finally, Houff and co-workers[41] recently reported on the case of a 37-year-old woman who died 50 days after keratoplasty using donor tissue from a 39-year-old rancher who had died in 22 days of a progressive neurologic disease. Subsequent investigation revealed that both the donor and recipient died of rabies.

In summary, there have been nine reported cases of the transmission of donor disease to the recipient (Table V). Of the six eyes with endophthalmitis, five had bacterial and one fungal. Five eyes were lost. The onset of the bacterial endophthalmitis varied from 10 to 48 hours after penetrating keratoplasty. In the first reported case, retinoblastoma was noted in the recipient 1½ years after keratoplasty. In the two cases of transmission of viral systemic disease, death occurred in 50 days in the case of rabies, and

TABLE V: TRANSMISSION OF DONOR DISEASE: SUMMARY

Total cases: 9

Cause: Endophthalmitis — 6
Bacterial — 5 (4 eyes lost)
Fungal — 1 (eye lost)
Retinoblastoma — 1 (eye lost)
Systemic viral diseases — 2 (both fatal)

Preservation: Moist chamber — 7
MK medium — 2

Onset of endophthalmitis: 10 hr to 2 mo

Death (2 cases): 50 days and 27 mo post-penetrating keratoplasty

in 27 months in the case of Creutzfeldt-Jakob disease. The preservation technique involved in the three cases of transmission of tumor and virus disease was moist chamber at 4 C. Of the six cases of endophthalmitis, two donor eyes had been preserved using intermediate-term storage techniques.

BACTERIOLOGIC SCREENING OF MEDICAL EXAMINER'S TISSUE

Background

Although there appears to be an increased number of reports in the literature of endophthalmitis following penetrating keratoplasty, the actual cause is not certain. Whether this increased incidence of infection is real or apparent is not clear. There are many possible factors. More penetrating keratoplasties are performed annually by ophthalmologists in the United States than ever before. The most recent study estimates that over 10,000 keratoplasties were done in 1978.[28] There are a variety of reasons for this increase in keratoplasties. The proliferation of eye banks has made good donor tissue more easily available. Improved surgical techniques such as the use of fine sutures and the operating microscope have increased the willingness of surgeons to operate. The indications for keratoplasty have changed. Consequently, aphakic bullous keratoplasty and previously failed grafts, which several decades ago were rarely operated on, now compose the majority of corneal transplants.[42] Moreover, there appears to be a greater willingness of surgeons to report their complications in the literature. The use of fine sutures that remain in the recipient for long periods may also influence the incidence of postoperative bacterial infection. The use of corticosteroids on a long-term basis in combination with modern suture techniques may also be a factor, particularly in the rare cases of fungal endophthalmitis.[43,44] Finally, the use of intermediate-term and tissue-culture preservation techniques may play a role in this apparent increased incidence of endophthalmitis following penetrating keratoplasty.[45]

In 1965, Rollins and Stocker[46] reported on conjunctival cultures taken prior to the application of Neosporin on 100 whole eyes enucleated by their eye bank. The eyes, subsequently, were used for keratoplasty. Positive bacterial cultures were obtained in 61% of the eyes. There were no immediate postoperative infections. However, they reported six infected grafts from one to six months after surgical treatment. Four were bacterial and two were fungal. In only one case did the organism match the positive donor culture, and this was a *Staphylococcus aureus*. Because this infec-

tion occurred 3½ months after surgical treatment, contamination of donor tissue was not believed to be a factor.

In 1967 Polack et al[47] reported 100% positive conjunctival cultures on 240 whole eyes, enucleated using standard aseptic precautions and sterile instruments, primarily at the Columbia Presbyterian Medical Center in New York. Most enucleations were done in the autopsy room from 4 to 14 hours after death. The cadavers had been at room temperature for four to eight hours preceding the enucleations. A solution of neomycin-polymyxin B, used to irrigate the cornea, notably reduced the incidence of positive cultures in the tissue.

Buxton and Brownstein[48] obtained 22% positive cultures on corneal epithelium from 100 donor eyes that had been treated with thimerosal prior to penetrating keratoplasty. Although one half of the positive cultures were considered "potentially pathogenic," there were no infections in the recipient eyes.

Keates et al[49] reported on ten pairs of donor eyes taken from patients with terminal systemic infections. All eyes were treated as potential donors. One cornea of each pair (group A) was excised and placed in commercially available MK medium containing 100 units of penicillin and streptomycin per milliliter. After 24 hours in the MK medium, the whole cornea was then placed in thioglycollate culture medium and incubated at 37 C. The fellow eye (group B) was stored in a moist chamber at 4 C. Three days after enucleation, the cornea was excised and placed in thioglycollate. All cultures were checked daily over a two-week period. Positive bacterial cultures of the corneas were found in 30% of those stored in MK medium for 24 hours compared with 40% of those stored in a moist chamber for 72 hours. In addition, aqueous cultures were taken in all 20 eyes at the time the cornea was excised. The aqueous cultures were positive in three of the seven eyes that had a positive corneal culture, suggesting diffuse ocular contamination in septicemia. In a similar study of 25 corneas from nonseptic donors stored in MK medium, all had negative cultures.[50]

Mascarella and Cavanagh[51] recently reported on 200 consecutive keratoplasties in which the residual MK solution was cultured postoperatively. There were positive cultures in 14% of the residual scleral rims and in 2.5% of the residual MK solution. Despite this incidence of positive cultures, there were no cases of postoperative infection in the recipients.

The MEB was the first to collect donor corneas on a routine basis from the Medical Examiner's office and to preserve these on an intermediate-term basis in MK solution prior to keratoplasty. To decide whether routine conjunctival cultures taken on this source of donor material would be worthwhile, the following study was undertaken.

TABLE VI: RESULTS OF CULTURES

	Group A postpreparation	Group B		Groups A and B postpreparation
		Prepreparation	Postpreparation	
No growth	60.0%	24.0%	78.0%	69.0%
Bacteria	40.0%	76.0%	22.0%	31.0%
Fungi	1.5%	1.5%	1.5%	1.5%

Material and Methods

Preoperative conjunctival cultures were taken on 134 potential donor eyes at the Medical Examiner's office by personnel of the MEB. These corneas were preserved in MK solution, and 127 of them were subsequently used for keratoplasty. Group A cultures were done between March 1977 and June 1978 and group B between December 1978 and February 1979. In group A, 67 conjunctival cultures were obtained after the routine preparation and polymyxin B-neomycin gramicidin (Neosporin) soak. The corneas and scleral rims were then removed and preserved in MK solution. Group B comprised the other 67 donor eyes. In these donors, conjunctival cultures were obtained both before and after the routine preparation and Neosporin soak. All cultures were taken with a sterile swab and incubated in MK medium without antibiotics at 36 to 37 C. If no turbidity was observed after two weeks of incubation, the cultures were classed as negative. If growth was noted, the culture tubes were then sent to the Johns Hopkins Hospital Bacteriology Laboratory for identification.

Results

In group A cultures taken after the preparation, positive bacterial cultures were obtained in 40% and *Candida* was cultured in one eye (Table VI).

In group B, cultures were obtained both before and after the routine preparation and Neosporin soak. Positive bacterial cultures were present in 76% initially and reduced to 22% postpreparation (Table VI).

Combining the postpreparation cultures of groups A and B for a total of 134 eyes, there was an incidence of 31% positive bacterial cultures in 42 eyes (Table VI). Cultures were positive for *Candida* in one case of group A and one case of group B for an overall incidence of 1.5%.

The nature of the positive prepreparation cultures is shown in Table VII. *Staphylococcus epidermidis* and *Streptococcus viridans* each composed approximately 35% of the positive cultures. *Diphtheroids*, *S aureus*, *Escherichia coli*, and *Acinetobacter* were the next most frequent bacteria found. *Pseudomonas* was found in 10%. *Candida* was found in one eye, or 2% of the positive prepreparation cultures.

TABLE VII: POSITIVE PREPREPARATION CULTURES: 51 EYES

Culture	Incidence	%
Bacteria		
Staphylococcus epidermidis	18	35.3
Streptococcus viridans	18	35.3
Diphtheroids	7	13.7
Staph aureus	7	13.7
Escherichia coli	7	13.7
Acinetobacter sp	7	13.7
Enterobacter sp	6	11.8
Bacillus sp	5	9.8
Pseudomonas sp	5	9.8
Strep group D (enterococcus)	4	7.8
Klebsiella pneumoniae	2	3.9
Neisseria sp	2	3.9
Proteus mirabilis	2	3.9
Strep pneumoniae	2	3.9
β-streptococcus sp	2	3.9
Aerococcus viridans	1	2.0
Citrobacter freundii	1	2.0
Peptococcus sp	1	2.0
Light yellow pigmented organism	1	2.0
Fungi		
Candida tropicalis	1	2.0

The nature of the positive postpreparation cultures is shown in Table VIII. *Streptococcus viridans* and *S epidermidis* again made up the bulk of the positive cultures, with an incidence of 33% and 29%, respectively. The next most frequent bacteria found were *E coli*, *Acinetobacter* sp, and *Pseudomonas*. Occasionally, a single eye was positive for several different bacteria. *Candida* was present in two postpreparation cultures for a total incidence of 5% in the positive postpreparation cultures.

Of this series of 134 potential donors, 127 corneas were sent out and used for keratoplasty. Of these, 43 were used locally; 77, elsewhere in the United States; and 7 were sent overseas. Our follow-up on these keratoplasties ranges from two months to two years. There was one case of bacterial endophthalmitis caused by a β-hemolytic streptococcus that occurred 36 hours after surgery. The eye was refractory to therapy and was lost. The donor had died without evidence of infection or sepsis, and the conjunctival culture of the donor cornea was negative. The other cornea of the pair was likewise culture-negative and was transplanted without complication.

Discussion

Because of the increased use of MK medium for intermediate-term storage of donor tissue, quality control is extremely important. The increased

TABLE VIII: POSITIVE POSTPREPARATION CULTURES: 42 EYES

Culture	Incidence	%
Bacteria		
Streptococcus viridans	14	33.0
Staphylococcus epidermidis	12	29.0
Escherichia coli	3	7.0
Acinetobacter sp	3	7.0
Pseudomonas sp	3	7.0
Diphtheroids	2	5.0
Klebsiella pneumoniae	2	5.0
Strep group D (enterococcus)	2	5.0
Staph aureus	1	2.5
Bacillus sp	1	2.5
β-streptococcus sp	1	2.5
CDC-VE-2*	1	2.5
Enterobacter sp	1	2.5
Micrococcus sp	1	2.5
Proteus mirabilis	1	2.5
Fungi		
Candida albicans	1	2.5
C tropicalis	1	2.5

*Center for disease control unnamed nonfermenting gram negative rod.

handling of donor tissue by eye bank technicians necessitated by this method of preservation increases the potential margin for contamination of the donor tissue or damage to the donor endothelium or both. However, no consensus has been reached on whether an eye bank should be responsible for the microbiologic screening of donor tissue. The cost for individual eye banks of culturing each respective donor eye is enormous. The question is whether universal microbiologic screening at the eye bank level would be cost-effective. Usually the results are not obtained until after the cornea has been sent out and used. There is also a significant percentage of false-positive cultures. If an infection does occur, surgeons prefer the microbiologic techniques of their own hospital in determining modes of therapy.

Routine preoperative conjunctival culture screening of all corneal donor tissue from the Medical Examiner's office would have eliminated approximately a third of the potential donor tissue. Also it would have forced a delay in the use of culture-negative tissue to the limits of our present methods of intermediate-term preservation. Consequently, we do not believe that the routine preoperative screening of corneal donor tissue by eye banks is warranted at the present time. However, when new eye banks are started, when new technicians are trained, or when new methods of collection are instituted, such as the program at the Medical Examiner's office, it would be prudent for an eye bank to do some preoperative conjunctival cultures to evaluate its own quality control. It also may be

advisable for eye banks to perform periodic consecutive conjunctival cultures on donor eyes to reassess their own techniques. *Culture of the residual cornea and MK medium in the operating room by the surgeon is strongly recommended.* If endophthalmitis does ensue, one could then be certain whether it came from the donor tissue or from contamination during processing, or both, or whether it occurred from other unidentified factors.

MANUAL OF POLICIES AND PROCEDURES

In 1977 the author and Dr Charles R. Graham, laboratory director of the MEB produced the first comprehensive manual for eye banking personnel, enucleation technicians, and corneal surgeons, including recommended policies, procedures, and guidelines relevant to obtaining, processing, and distributing human eye tissue for surgical procedures, teaching, and research. The manual gives specific recommendations for the selection of donor material as well as step-by-step instructions as to the techniques of modern eye banking, particularly the use of intermediate-term preservation with MK medium. Furthermore, this document was designed so that revisions could be made as new information became available. It has been distributed at home and abroad to eye banks and corneal surgeons that use tissue from the MEB. Presently, the Agency for International Development of the US Department of State is considering translating this manual into French and Arabic for use in establishing and improving eye banks in underdeveloped countries.

KERATOPLASTY PROJECT: LONG-TERM FOLLOW-UP IN KERATOCONUS

BACKGROUND

Accurate and periodic follow-up information is essential for an eye bank to assess its systems of quality control. It is also impossible to evaluate the key variables in keratoplasty without follow-up information. All the clinical reports that attempt to draw conclusions regarding the significance of donor age, time between death and enucleation, type of preservation, and preservation time require detailed follow-up information. In the past, these reports have generally come from individual surgeons in retrospective studies rather than from prospective studies by eye banks.

Short-Term Storage

Kaufman et al[52] compared the results obtained in penetrating keratoplasty of 24 donors in short-term storage up to 58 hours in moist chamber at 4 C

with 30 donors cryopreserved for up to six months. However, the recipient diagnoses varied considerably. The six-month follow-up showed no statistical difference between the two groups. Clear grafts were observed in 54% (11) of patients receiving short-term preserved donor tissue as compared with 47% (14) of patients receiving cryopreserved corneas. Saleeby[53] reported an 83% rate in 145 penetrating keratoplasties using donor tissue stored in moist chamber for 50 to 80 hours with a donor age from 50 to 85 years. The recipient diagnoses in this series were also variable. Dhanda and Kalevar[54] reported a success rate of 54% in penetrating keratoplasties using donor tissue stored in moist chamber for 4 to 58 hours.

Moist chamber preservation has been studied by numerous authors in vitro using light microscopy,[55] transmission and scanning electron microscopy,[56-58] temperature reversal,[59] trypan blue[58] and nitroblue tetrazolium staining,[55] and most recently, specular microscopy.[60] McKinnon and Walters,[59] studying temperature reversal in rabbits, showed that the length of time a cornea remains in a cadaver may be another important factor in endothelial viability. The general recommendation from these studies has been that the maximum short-term storage in moist chamber preservation of human corneal donor tissue is 48 to 72 hours.

Intermediate-Term Storage

Magitot,[14] in 1911, was the first to store donor cornea in hemolyzed serum prior to keratoplasty. Fifty-seven years later, Stocker[61] used donor corneas stored in recipient serum for 100 hours. Kuwahara et al[62] reported from Japan in 1965 on 400 cases of keratoplasty using intermediate-term storage for up to seven days in a special medium. McCarey and Kaufman[32] introduced their intermediate-term storage medium in this country in 1974. Since then there has been an increasing use of MK storage in the United States, although only a few clinical studies[63-67] have demonstrated the efficacy of this technique with adequate follow-up (Table IX). These reports either involve small numbers of cases or have a variety of recipient diagnoses.

Because of enthusiastic reports of favorable results from several local surgeons using MK-preserved donor tissue, the MEB began using this storage technique on a routine basis in 1974. Beginning in July 1975, with the Medical Examiner's law in effect, this technique was used exclusively for the storage of corneas obtained from the Medical Examiner's office. Since 1974 the laboratory personnel of the MEB have been making our own MK media for intermediate-term storage in order to assure its quality control. It should be noted that there have been recent reports of possible

TABLE IX: CLINICAL USE OF M-K-STORED DONOR CORNEAS

Author	Date	Total no. of PK*	1° failures	Donor storage time		% Success		Average follow-up
				0-72 hr	73-270 hr	0-72 hr	73-270 hr	
Bigar et al[63]	1975	28	1	18	10	94	70	2.0 mo
Stark et al[64]	1975	57	1	53	4	92	75	3.7 mo
Aquavella et al[65]	1975	25	0	25†	. . .	92	. . .	4.7 mo
McCarey et al[66]	1976	92	0	68	24	74	54	18.0 mo
Stainer et al[67]	1979	21	0	21	. . .	95	. . .	18.0 mo

*PK = Penetrating keratoplasty.
†Used 68 to 80 hours after donor death.

TABLE X: CLINICAL REPORTS ON PENETRATING KERATOPLASTY FOR KERATOCONUS

Date	Author	No. of PK*	Donor information	% success	Follow-up
1948	Owens et al[68]	63	Variable	65	4 mo or more
1953	Paton[69]	84	Variable	89	2 mo or more
1969	Buxton et al[70]	36	60 yr old or less 24 hr PM† or less	94	6 wk
1969	Anseth[71,72]	70	. . .	94	. . .
1971	Forster and Fine[73]	132	95%, 48 hr PM or less	89	6 mo or more
1971	Moore and Aronson[74]	12	. . .	100	9 mo or more
1972	Stark et al[75]	30	60 yr old or less 24 hr PM or less	95	6 mo or more
1972	Keates and Falkenstein[76]	27	. . .	100	1-6 yr
1974	Chandler and Kaufman[77]	53	Cryopreserved and fresh	90	3 yr
1979	Forster[78]	25‡	Average 17 hr PM	72	24 mo average
1979	Donshik et al[79]	124		90	18 mo average

*PK = Penetrating keratoplasty.
†PM = Post mortem.
‡Includes Fuch's and other corneal dystrophies.

problems with the quality control of the commercial MK medium imported by some eye banks from Laboratories Eurobio, Paris. Early graft failure has occurred in some cases (S. R. Waltman, MD, Nov. 1979 oral communication).

Keratoconus

Keratoconus has long been known to have the best prognosis in penetrating keratoplasty (Table X).[68-79] It varies from 65% in the early series by Owens et al[68] to 90% in the recent series by Donshik et al.[79] All these series used donor tissue preserved by short-term techniques. Because of the infrequency of complicating factors such as glaucoma and neovascularization and the resultant high success rate, keratoconus remains the ideal recipient disease in which to assess various other factors that may influence the outcome of penetrating keratoplasty.

MATERIALS AND METHODS

In 1974 the MEB began a project to assess the key variables of corneal donor tissue by obtaining long-term follow-up data on recipients. Table XI lists the kinds of information that was sought. Pertinent information on the

TABLE XI: INFORMATION ON EACH CASE

Donor	Recipient	Follow-up
Technician	Hospital	Vision
Source	Surgeon	Corneal status
Culture	Phakic or aphakic	Cause of visual acuity if < 20/40 and cornea clear
Disposition	Date-time of transplant	Rejection
Age, race, sex	Age, race, sex	Complications postoperatively
Date-time	Vision	Average number of PKs per year by surgeon
Death-enucleation	Diagnosis	
Death-preservation	Ocular status other eye	
Cause of death	Previous PK* (donor or recipient)	
Type of preservation	Neovascularization	
Corneal status	Glaucoma	
	Medical problems	
	Previous transfusions	
	Previous pregnancies	
	Emergency or elective	
	Preoperative estimate of success	
	Full thickness or lamellar	
	Graft size	
	Combined with cataract extraction	
	Suture size and type	
	Suture technique	
	Microscope	
	Operative complications	

*PK = Penetrating keratoplasty.

donor was recorded at the MEB. The surgeon was requested to complete a form at the time of surgery giving information on the recipient and surgical technique. Of approximately 5,000 keratoplasties performed between 1974 and 1978 using donor tissue from the MEB, 410 cases had a recipient diagnosis of keratoconus. Long-term follow-up information was then requested on these cases. The data were then analyzed by computer.

RESULTS

Of the 410 cases of keratoconus, the author was able to obtain postoperative follow-up of six months or more on 390 cases (95%). The charts of 80 of the local cases were reviewed by the author (21%). Information was obtained directly from patients or their families in 47 cases (12%). The case was personally discussed with the operating surgeon in 79 cases (20%). Follow-up information in 93 cases (24%) was obtained from other ophthalmologists or, in a few instances, from optometrists who had seen the patients. In the remaining 23% of cases, the follow-up information was obtained solely from the follow-up forms filled out by the surgeon. The average length of follow-up in these cases was 23 months. Consequently, it is believed that the following results represent good data. It might be expected that some complications and homograft reactions would not be reported, and therefore their frequency may tend to be underestimated. However, the author was impressed with the overall cooperation and candor of the many ophthalmologists who participated.

Of these 390 cases in which adequate follow-up information was obtained, there was a large group of 322 cases in which the recipient eye was phakic without previous keratoplasties on the recipient eye, and a penetrating keratoplasty was done for the improvement of vision. The results in this group of 322 cases was compared in Table XII with the results in four other recipient eye groups, ie, those with one previous penetrating keratoplasty on the recipient eye, those with two or more previous penetrating

TABLE XII: RESULTS IN DIFFERENT RECIPIENT EYE GROUPS (362 CASES)

	No. of cases	% Clear	% Homograft reactions
No previous surgery	322	93	10
One previous PK*	21	81	10
Two or more PKs	6	67	17
Aphakic, no PK	8	88	25
Lamellar	5	40	0
		$P < .01$	$P = .5$

*PK = Penetrating keratoplasty.

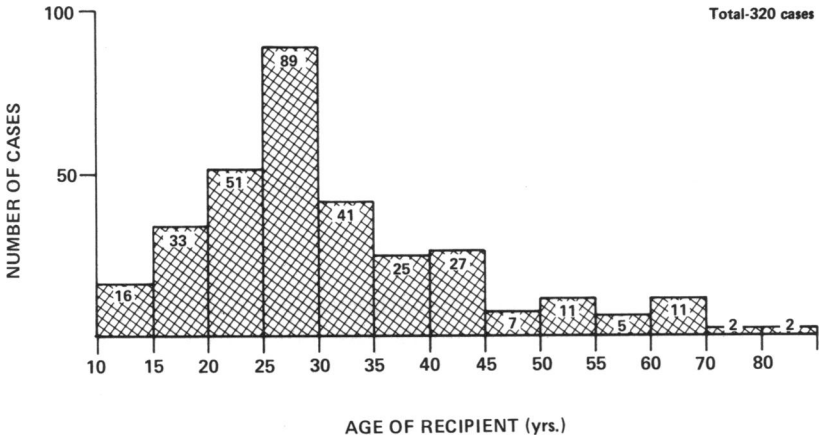

FIGURE 1
Recipient age in 320 cases of keratoconus.

keratoplasties, those who were aphakic but with no previous penetrating keratoplasties, and those on whom a lamellar graft was done as the initial procedure. The group with no previous surgical treatment on the recipient eye had a 93% incidence of clear grafts. There were significantly lower success rates in the other groups ($P < .01$). The incidence of homograft reactions (including those resulting in graft failure as well as those successfully treated) in the various groups also is shown in Table XII. Statistically there was no significant difference among the groups ($P = .5$).

The remainder of the results reported here are limited to the group of 322 cases without previous surgical treatment on the recipient eye. The donor tissue was obtained from the Medical Examiner's office in 197 cases and from hospitals and other sources in 125 cases (Table XIII). Of the 125 whole donor eyes, 71 were preserved by moist chamber at 4 C. All tissue

TABLE XIII: RESULTS AS TO PRESERVATION TYPE (322 CASES)

Preservation	No. of eyes	Donor age (mean in yr)	Time*			% Clear
			D-E	D-P	D-T	
Moist chamber	71	53	3.4	3.4	30.6	90
MK medium	251	32	3.5	5.7	43.8	94
Medical Examiner	197	28	. . .	5.3	42.3	95
Others	54	46	3.5	7.1	49.0	89
Overall						93

*Mean in hours. D-E = death-enucleation; D-P = death-preservation; D-T = death-transplant.

from the Medical Examiner's office (197 cases) was preserved immediately in MK intermediate-term storage medium. The other 54 donor eyes were originally enucleated, and several hours later at the MEB, the cornea was excised with a rim of sclera and then preserved in MK medium. The donors were male in 75% (240/319) of cases and white in 60% (191/319) of cases. The average age of eyes obtained from hospitals and stored in MC was 53 years, compared with an average age of 28 years in tissue from the Medical Examiner's office. Because most autopsies at the Medical Examiner's office involve trauma, the causes of death in 51% (163/322) of cases were accidents, homicide, or suicide.

The death-enucleation time in eyes preserved in moist chamber is often the same as the death-preservation time, because moist chamber preservation is usually begun at the time of enucleation. In Medical Examiner's cases, only the cornea is removed and then preserved immediately in MK medium. Consequently, there is only a death-preservation time in this group. In some donor eyes initially preserved in moist chamber, the corneas were later excised and preserved in MK medium. Hence, there are both a death-enucleation time and death-preservation time in these cases. The death-enucleation time averaged three hours in the 71 eyes preserved in moist chamber, while the death-preservation time averaged five hours in the Medical Examiner's cases (Table XIII).

Of the 322 cases, 85 penetrating keratoplasties were performed locally; 208, elsewhere in the United States; and 29, overseas. There were 120 different surgeons. Each performed between one and 30 transplants in the series. The average death-transplant time was 40.9 hours. The age of the recipients varied from 10 to 84 years with 72% being 35 years or younger. The recipients were male in 60% (191/320) of cases. White males constituted 51% (165/320); white females, 24% (78/320); black females, 11% (35/320); and black males, 5% (16/320) of cases. In 85% of cases the keratoconus was bilateral. Previous penetrating keratoplasties had been performed on the other eye in 82 cases. Glaucoma was present preoperatively in only three cases and neovascularization of the cornea in only seven cases. Medical problems were present in 13% (42/322) of cases (Table XIV). Down's syndrome was present in nine cases. Only two cases were known to have had previous transfusions, and 43 cases were known to have had previous pregnancies.

The keratoplasty was categorized by the surgeon as elective in 98% and done for improvement of visual acuity in 100%. The preoperative estimate of success by the surgeon was listed as 75% or better in 96% of the cases. Donor graft size, known in 309 cases, varied between 6.5 and 9.0 mm. The recipient graft size was smaller in 19 cases. Surgical therapy was combined

TABLE XIV: MEDICAL PROBLEMS (42 OF 322 CASES)

Nature	No. of cases
Down's syndrome	9
Hypertension	5
Diabetes	2
Blood dyscrasias	2
Cancer	1
Minor problems	23
Total	42 (13%)

with cataract extraction in four cases. The suture size was 10-0 in 93% (295/319) of cases. Silk was used in only 11 cases. A running suture was used in 51% (162/317); interrupted, in 14% (45/317); and a combined technique, in 35% (110/317) of cases. Surgeons used the microscope in 95% (304/319) of cases. Operative complications were reported in 3% (9/322) of cases (Table XV).

In the follow-up forms, corneal status was graded as clear, hazy, or opaque. Clear grafts were obtained in 93% (300/322) of cases (Table XIII). The success rate, as determined by clear grafts, between moist chamber and MK preservation was 90% and 94% respectively, values not significantly different ($P = .4$). In this series, donor age was not found to be a significant determinant of graft clarity. Of the 23 cases of graft failure, status recorded as hazy or opaque, nine cases were caused by rejection (Table XVI). These rejections occurred from five weeks to 14 months following keratoplasty (Table XVII). Primary donor failure was listed as the cause in six cases (Table XVIII). The incidence of primary donor failure in

TABLE XV: COMPLICATIONS AT SURGERY (9 OF 322 CASES)

Unplanned ECCE with vitreous loss	1
Cloudy graft replaced with backup	1
Air behind iris, difficulty forming anterior chamber	1
Trephine damage to iris	1
Hyphema	1
Poor exposure, tight orbit	1
Subconjunctival hemorrhage from injection	1
Broken running suture	2
Total	9 (2.8%)

TABLE XVI: CAUSE OF GRAFT FAILURE (23 OF 322 CASES)

Rejection	9
Primary donor failure	6
Technical problems at surgery	3
Corneal ulcer	2
Pupillary block with intumescent lens	1
Endophthalmitis	1
Herpes in graft	1
Total	23 (7.1%)

moist chamber and MK preservation was 1.4% and 2.0%, respectively. Failures were attributed to technical problems at surgery in three cases (Table XIX).

Both the preoperative and postoperative visual acuities were known in 308 cases (Fig 2). The postoperative visual acuity was recorded as 20/40 or better in 79% (244/309) of these cases. Visual acuity in those with a clear graft was less than 20/40 in 17% (54/322) of cases (Table XX). Postoperative astigmatism, varying from +4.5 to +18.0 diopters, was responsible for the decreased vision in 15 of these cases. Irregular astigmatism was present in six of the 15 cases. Successfully treated homograft reactions were reported in 7.1% (23/322) of cases (Table XVII). Previous penetrating keratoplasty on the other eye (82 cases) did not significantly affect the incidence of homograft reactions or graft failure.

There were 77 instances of postoperative complications other than graft failure (Table XXI). These involved 18.6% (60/322) of cases. A subsequent operative procedure was necessary in 4.7% (15/322) of these cases that did not fail. Cataracts occurred in 11 cases, five of which required cataract surgery. Postoperative trauma occurred in six cases, three of which had a loss of the lens and vitreous (Table XXII). One of these cases required two operations for a subsequent retinal detachment.

When graft clarity was evaluated as to geographic area (Table XXIII), there was a significant reduction in the success rate overseas compared with the success rate locally and elsewhere in the United States ($P < .01$).

TABLE XVII: HOMOGRAFT REACTIONS (32 OF 322 CASES)

	No. of cases	Onset	Incidence
Graft failures	9	5 wk-14 mo	2.8%
Other rejections	23	1 wk-2½ yr	7.1%
Total	32		9.9%

TABLE XVIII: PRIMARY DONOR FAILURE (6 OF 322 CASES)*

	Donor					Recipient		
Date of surgery	Age, race, sex	Cause of death	Preservation	Death to PK† time (hr)	Mate	Age, race, sex	Preoperative vision	No. PK per yr by surgeon
July 1974	75, W, M	Cardiovascular arrest	MK	116	Not used	12, W, M	HM‡	24
August 1974	59, B, M	Cancer	MK	65	Clear	23, W, M	CF§	25
June 1976	71, W, F	Cancer	MC‖	18	Clear	41, B, F	CF	110
August 1976	38, B, F	Lupus	MK	58	6 mo to clear	29, W, M	CF	50
November 1977	24, W, M	Trauma	MK	59	Clear	20, B, M	CF	53
July 1978	22, B, M	Trauma	MK	54	Clear	20, W, F	20/400	6

*Incidence: moist chamber—1/71 (1.4%); MK—5/251 (2.0%).
†PK = Penetrating keratoplasty.
‡HM = Hand motions.
§CF = Counting fingers.
‖MC = Moist chamber.

TABLE XIX: TECHNICAL FAILURES (3 OF 322 CASES)

Date of surgery	Recipient			Nature of problem	No. of PK per yr by surgeon	Follow-up
	Age, race, sex	Preoperative vision	Previous PK*			
July 1975	16, W, F	<20/400	None	Flat AC† iris to wound	3	1976 repeat PK 1977 cataract removal 1979 vision = 20/40
October 1976	33, W, F	20/100	None	Wound problem and 2° infection	5	1978 Vision = 20/200
October 1977	13, W, M	CF‡	None	Air behind iris, trouble forming AC	12	1978 Vision = HM§

*PK = Penetrating keratoplasty.
†AC = Anterior chamber.
‡CF = Counting fingers.
§HM = Hand motions.

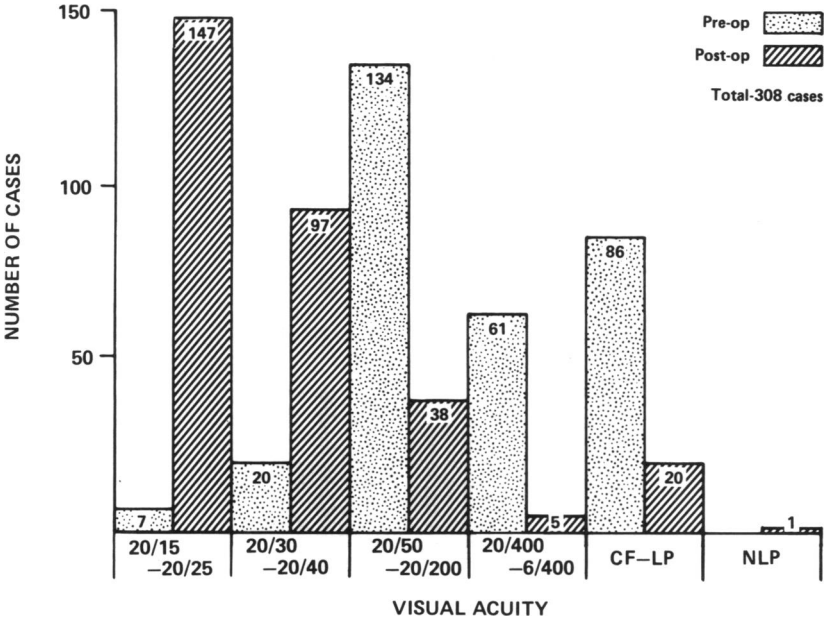

FIGURE 2
Preoperative and postoperative visual acuity in 308 cases of keratoconus with penetrating keratoplasty.

This lowered success rate in the overseas cases was probably related to the significant increase in the death-transplant time, which was a definite determinant of graft clarity ($P < .001$). One other factor determined graft clarity: the clear grafts were significantly smaller than those that failed, averaging 7.7 mm in the clear grafts compared with 7.9 mm in those that failed ($P < .05$).

Information on the average number of keratoplasties performed annually by the operating surgeon was obtained from the MEB and operating room records in the local cases and from the operating surgeon or his secretary in the others. The number varied from one case to 325 cases per year. Approximately 50% of the surgeons performed fewer than 23 keratoplasties per year. In 21 cases, the surgeon performed 100 or more corneal transplants per year. The average number of keratoplasties done annually was not a definite factor in graft clarity, although there was a higher failure rate in those cases in which surgeons performed fewer keratoplasties per year ($P = .18$) (Fig 3). Those surgeons who did fewer than five keratoplasties annually had a success rate of 88.4%, whereas those surgeons who performed 30 keratoplasties or more per year had a success rate of 95.9%.

TABLE XX: CAUSE OF VISUAL ACUITY <20/40 IN CLEAR GRAFTS (54 OF 322 CASES)

Cause	No. of cases
Astigmatism	15
Down's syndrome	9
Cataracts	6
Amblyopia	5
Glaucoma	3
Myopic degeneration	3
Cystoid macular edema	2
Other retinal disease	2
Nystagmus	1
Graft thinning	1
Unknown	7
Total	54 (17%)

Eighty-five local cases were analyzed as to graft clarity with respect to whether the surgeon was full-time, part-time, resident, or private (Table XXIV). The difference in success rates was not statistically significant between the groups. The postoperative complication rate was not significantly different among the various geographic areas or among the types of local surgeons. The rate of complications also was not related to number of keratoplasties performed annually.

TABLE XXI: POSTOPERATIVE COMPLICATIONS OTHER THAN GRAFT FAILURE (60 OF 322 CASES)

Type	No.	Reoperation	Nature
Homograft reactions	23	1	Laser to new vessels
Astigmatism (visual acuity <20/40)	15	1	Wedge resection
Cataracts	11	5	Cataract surgery
Glaucoma			
Pupillary block	2	1	Iridectomy
Other	5	1	Trabeculectomy
Trauma*	6	5	Resuturing
Infections			
Suture abscess	4	0	. . .
Corneal ulcer	1	0	. . .
Wound bulge	3	0	. . .
Cystoid macular edema†	3	0	. . .
Hyphema	2	0	. . .
Wound leak	1	1	Resutured
Late clearing (6 mo)	1	0	. . .
Total no.	77	15	
Total cases involved	60 (18.6%)	15 (4.7%)	

*3 cases—loss of lens and vitreous.
†2 cases—subsequent to cataract surgery.

TABLE XXII: POSTOPERATIVE TRAUMA (6 OF 322 CASES)

Date of surgery	Age, race sex	Recipient			Trauma		Follow-up
		Preoperative vision	Time postoperative	Nature	Sutures in place	Nature of surgery	
March 1975	15, B, M	20/200	2½ wk	Friend's elbow, accident	Yes	Resuturing, iris prolapse	Clear, 1979 Vision = 20/40
August 1975	30, B, M	20/100	2 mo	Fist fight	Yes	Resuturing, loss of lens and vitreous	Clear, retinal detachment ops ×2 1979 Vision = 20/200
April 1976	32, W, F	20/70	6 wk	Whiplash accident	Yes	None, shift in keratometer readings	Clear, 1979 Vision = 20/25
March 1977	33, W, M	20/300	5½ mo	Hit by infant daughter	2 days after removal	Resuturing	Clear, 1979 Vision = 20/30
May 1977	21, W, M	20/80	2 mo	Water skiing accident	Yes	Resuturing, loss of lens and vitreous	Clear, 1979 Vision = 20/25
July 1978	43, B, F	Hand motions	3 mo	Hit by grandson, accident	Yes	Resuturing, loss of lens and vitreous	Clear, 1979 Vision = 20/100, high astigmatism

TABLE XXIII: RESULTS AS TO AREA (322 CASES)

	No. of cases	% Clear	D-T time (mean)*
Local	85	95	38.1
USA	208	94	35.3
Overseas	29	79	89.6
		$P<.01$	$P<.001$

*D-T = Death-transplant.

DISCUSSION

This prospective comprehensive study of primary penetrating keratoplasty in keratoconus is the first of its kind undertaken by an eye bank. The overall success rate (clear grafts) of 93% compares favorably with the success rate previously reported in individual series (Table X). The use of intermediate-term preservation techniques (MK) and the use of the Medical Examiner's office as a source of donor tissue yield results equal to, if not slightly better than, the results obtained using moist-chamber storage (Table XIII). Primary donor failure, which has been shown to be caused by an inadequate endothelium[80] occurred in only 1.6% of MK-preserved donor tissue compared with 2.8% of moist chamber-preserved donor tissue. Thus, there was no notable increase in endothelial damage from the intermediate-term processing by eye bank technicians.

It was anticipated in this large series that donor age would be a determinant of graft clarity. The data, however were not significant in this respect, and thus this report collaborates the results of other smaller series.[73,78,81] This result may be due to the fact that the average age of donor tissue obtained from the Medical Examiner's office was 28 years and thus was relatively young tissue.

Graft clarity was related to the death-transplant time in the overseas cases but not in those done in the United States (Table XXIII). The mean death-transplant time on cases done locally and elsewhere in the United

TABLE XXIV: RESULTS OF LOCAL SURGERY (85 CASES)

	No. of cases	No. of surgeons	% Clear
Full-time	55	3	98
Part-time	11	7	91
Residents	13	13	92
Private	6	6	83
		$P = .08$	

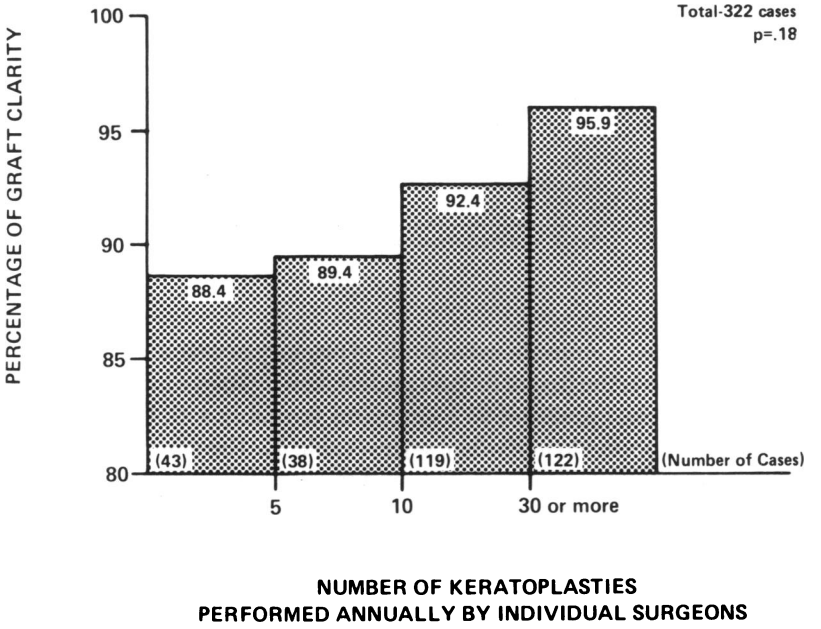

FIGURE 3
Relationship of graft clarity to number of keratoplasties performed annually by individual surgeons.

States was less than 40 hours, compared with a mean death-transplant time of 90 hours in the overseas cases. This significantly lowered the success rate in the overseas cases. This may be related to the difficulty in maintaining the temperature at 4 C in shipping overseas. In the future, donor tissue shipped overseas in MK medium should be used as soon as possible, preferably within 48 hours of death. Neither the death-enucleation nor death-preservation time had any significant effect on graft clarity. However, these times averaged less than six hours for both moist chamber and MK preservation.

Donor size was a significant determinant of graft clarity, with the smaller grafts having a greater chance of success. These results support other studies in which the incidence and severity of rejections were believed to be related to the size of the keratoplasty.[82,83]

It has been assumed by many that the success of a surgical technique is related to some extent to how frequently it is performed by an individual surgeon. This study tends to relate graft clarity to the average number of keratoplasties performed annually by the operating surgeon (Fig 3), although the results are not statistically significant.

The importance of homograft reaction to graft clarity was first emphasized by Maumenee.[84] In this series the incidence of graft failure from homograft reactions was 2.8%, and of overall homograft reactions, 9.9%. This is somewhat less frequent than the incidence of homograft reaction to keratoconus reported by others.[77,79] Moreover, there was no significant increase in the incidence of homograft reactions or graft failure in the 82 cases that had had previous penetrating keratoplasties on the other eye. These results do not confirm the increased incidence of homograft reactions in bilateral cases as reported by Donshik et al.[79]

Despite the high success rate, 17% of the clear grafts resulted in vision of less than 20/40. The astigmatism, 15 cases, could not be related to donor size, suture type, suture size, or suture technique, confirming the observations of others.[85,86]

Of particular interest in those whose grafts remained clear was the high incidence of postoperative complications, 19% (60/322) of cases (Table XXI). If one were to include those 23 cases with graft failure, 26% (83/322) of all cases had some postoperative problems. In the group with clear grafts and complications, 4.7% (15 cases) required further surgical treatment. Of the 23 cases with graft failure, ten cases were known to have undergone repeat keratoplasty, the case of endophthalmitis was eviscerated, and one case required repair of a leaking wound. Including these 12 cases, the overall incidence of subsequent surgery was 8.4% (27/322) of cases. This high incidence of postoperative complications and subsequent surgery reflects the overall experience of the patient population to primary penetrating keratoplasty for keratoconus better than previously published reports.[68,79]

RECOMMENDATIONS

This paper supports the contention that the Medical Examiner's office is a reliable source of excellent donor tissue for keratoplasty. Intermediate-term storage in our experience is a safe, effective method of preserving donor tissue. It is hoped that in the near future more states will enact similar laws to the one passed initially in the State of Maryland. Then more cost-effective regional eye banks can be formed. They will have a constant source of excellent donor tissue obtained from Medical Examiner's offices and preserved for up to 48 hours or more, using intermediate-term storage techniques. The vast majority of keratoplasties will become elective, scheduled procedures.

Furthermore, the use of this intermediate-term preservation technique can be readily combined with HL-A tissue typing in regional centers should histocompatibility prove to be another important factor determin-

ing graft clarity.[83,87] Routine use of specular microscopy for evaluating donor tissue also can be done more effectively in large sophisticated eye banks should this prove to be an important adjunct in the selection of donor tissue.[88]

Although the ultimate responsibility for the use of any donor tissue rests with the operating surgeon, eye banks are appreciating more than ever before the significance of their role in quality control. Systematic follow-up information is critical in this regard. Eventually certification procedures should be instituted among eye banks so that high standards can be maintained. This is particularly important for eye banks that use intermediate-term storage techniques.

The following recommendations are made to eye banks and corneal surgeons with respect to donor criteria:

ABSOLUTE CONTRAINDICATIONS TO USE

If any of the following are *known* to be present in the donor, the eyes should not be offered by the eye bank for surgery:

1. Disease of obscure or unknown etiology[89]
2. Creutzfeldt-Jakob disease[35,36,90]
3. Rabies[41]
4. Congenital rubella[91,92]
5. Subacute sclerosing panencephalitis[90,93,94]
6. Progressive multifocal leukoencephalopathy[90]
7. Subacute encephalitis from cytomegalovirus[95,96]
8. Other disseminated viral infections[90]
9. Septicemia[38-40,97]
10. Hepatitis or jaundice[90,98]
11. Blast forms of leukemia[97,99]
12. Intrinsic eye disease
    a. Retinoblastoma[34] or known malignant tumors of the anterior segment
    b. Active blepharitis or conjunctivitis
13. Slowly debilitating neurologic diseases or mental deterioration (may be caused by as yet unknown slow viruses)[89,90]

POSSIBLE CONTRAINDICATIONS TO USE

The MEB strongly recommends that any tissue with known intraocular pathologic condition or previous intraocular surgical therapy or both be reserved for ocular pathologic studies.

If any of the following are *known* to be present in the donor, the surgeon may want to reject the tissue:

1. Leukemia, other than blast form, and other blood dyscrasias[97,99]
2. Cancer with metastasis[97,100]
3. Syphilis
4. Tuberculosis
5. Hodgkin's disease and lymphomas
6. Chronic debilitating diseases; may be prone to terminal infections[40]
7. History of extensive terminal life support or hypothermia; may be prone to unrecognized sepsis[38]
8. History of immunosuppressive or corticosteroid therapy[39]
9. Diabetes[101]
10. Amyotrophic lateral sclerosis[102]
11. Multiple sclerosis[89,90]
12. Reye's syndrome[103]

If the donor is *known* to have any of these conditions, this information should be communicated to the surgeon when the tissue is offered. The final decision whether to use the tissue or not rests with the operating surgeon.

AGE OF DONOR

No donor age limits have been universally accepted for corneal tissue. The present study was unable to demonstrate a definite relationship between donor age and graft clarity. However, most surgeons prefer tissue under 65 years of age, although older tissue is sometimes used, especially in emergency situations. Many surgeons prefer to use young donor material for young recipients, but do not hesitate to use corneas from older donors for elderly recipients. Because donor tissue from infants is soft and technically difficult to use, many surgeons prefer not to use donor tissue from infants and very young children.

INTERVAL BETWEEN DEATH AND ENUCLEATION OR PRESERVATION

There is no consensus about the maximum acceptable interval between death and enucleation or preservation. Much depends upon the cause of death, the condition of donor tissue, and the temperature of the cadaver. Although clear grafts have been obtained using corneas with much longer intervals between death and enucleation, optimal tissue quality in the present study was obtained within six hours of death.

INTERVAL BETWEEN DEATH AND TRANSPLANT: PRESERVATION GUIDELINES

Most surgeons prefer to use fresh whole eyes kept in a moist chamber at 4 C within 24 hours after the death of a donor. Historically, however, this tissue has been used in the United States after storage of up to 72 hours. Reports from abroad indicate that clear grafts can be obtained after more than 72 hours' storage.[53]

Tissue from a previously healthy donor, when preserved by intermediate-term storage techniques (MK) may be acceptable well after 72 hours' storage. However, this study shows a significant deleterious effect on graft clarity in overseas cases in which the death-transplant time was more than 48 to 72 hours. Overseas surgeons are advised to use tissue preserved in MK from the United States within 72 hours for best donor quality.

Methods for the long-term preservation of viable corneal tissue are either experimental or difficult. Human corneas have been organ-cultured.[45] It is best to wait until more information is generated about the potential use of this tissue. Corneas frozen in excess of a year have been successfully transplanted; some corneal surgeons still use cryopreserved donor tissue.[52] Glycerin-preserved corneas, usually suitable for lamellar grafts only, have been stored for years.

SUMMARY AND CONCLUSIONS

The historical relationship between corneal surgery and eye banks has been reviewed and the development of eye banking in this country discussed.

The present-day concerns of eye banking have been analyzed and the following conclusions reached:

1. Funding of processing costs by third-party insurers has become an important source of financial support for eye banks.

2. The Medical Examiner's office has become an effective legal source of donor corneal tissue in the State of Maryland. This tissue, retrieved and preserved by technicians of the MEB using intermediate-term preservation techniques, is excellent and at least equal to donor tissue from whole eyes in short-term storage. There was no notable increase in the primary donor failure rate using intermediate-term storage. When similar laws are passed in other states, regional eye banks will be able to provide a constant source of excellent donor tissue so that most keratoplasties can be scheduled on a truly elective basis.

3. Quality control within eye banks is essential to provide safe donor tissue of high quality. Intermediate-term preservation techniques require strict standards of quality control. Preoperative conjunctival cultures of

donor eyes from the Medical Examiner's office are not recommended on a routine basis. Systematic follow-up procedures by individual eye banks on their donor tissue are essential for evaluting quality control.

4. Primary penetrating keratoplasty in keratoconus in a prospective series of 322 cases with a follow-up of six months or more (average 23 months) has a success rate, as determined by graft clarity, of 93%. Results were equally excellent with short-term and intermediate-term preservation techniques. Graft clarity was significantly reduced in overseas cases by a death-transplantation time of more than 72 hours. Donor age was not a significant determinant of graft clarity in this study. The size of the keratoplasty significantly influenced graft clarity. Despite the high success rate in this series, there was a significant rate of complications other than graft failure (19%) and reoperation (8%). This series probably better reflects the overall experience of patients with surgical therapy for keratoconus than prevous reports.

Finally, the story of eye banking provides a worthy illustration of how the cooperation of physician, scientist, paramedical personnel, and technologist may lead to the advancement of knowledge in a specific field with benefit to both patient and physician.

ADDENDUM

A tenth case of transmission of donor disease to a recipient via corneal transplant has been recently reported. On November 28, 1979 a 36-year-old man from France died of rabies 49 days following a penetrating keratoplasty for keratoconus. Thirty-three days after the transplant he complained of influenza-like symptoms and left retro-orbital headache. Progressive quadriparesis, dysarthria, and cerebellar dysmetria developed prior to a final coma. Rabies virus was isolated from the brain tissue at autopsy. The donor had been a 57-year-old woman, a long time resident of Egypt, who had lived in France for two months before the onset of her illness. She had died with a three week progressive flaccid quadriplegia syndrome. Upon discovery of rabies in the recipient, histologic and electron-microscopic examination of the donor's brain revealed the presence of numerous Negri bodies. This case was reported in the Morbidity & Mortality Weekly Report, Center for Disease Control, US Department of Health, Education, and Welfare/Public Health Service, Vol 29, No 3, Jan 25, 1980, p 25-26.

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APPENDIX

1979 CUMULATIVE SUPPLEMENT **§ 4-512**

Subtitle 5. Maryland Anatomical Gift Act.

§ 4-509.1. When Chief Medical Examiner or his deputy or assistant may provide cornea for transplant.

(a) *Requirements.* — In any case where a patient is in need of corneal tissue for a transplant, the Chief Medical Examiner, the deputy chief, or an assistant medical examiner may provide the cornea upon the request of the Medical Eye Bank of Maryland, Incorporated under the following conditions:

(1) A decedent who may provide a suitable cornea for the transplant is under his jurisdiction and an autopsy will be required in accordance with Article 22 of the Code;

(2) No objection by the next of kin is known by the medical examiner; and

(3) The cornea for transplant will not interfere with the subsequent course of an investigation or autopsy or alter the post mortem facial appearance.

(b) *Liability of medical examiner.* — Neither the Chief Medical Examiner, the deputy chief, an assistant medical examiner, nor the Medical Eye Bank of Maryland, Incorporated is liable for civil action if the next of kin subsequently contends that his authorization was required. (1975, ch. 73.)

Editor's note. — Section 2, ch. 73, Acts 1975, provides that the act shall take effect July 1, 1975.

§ 4-512. Short title.

This subtitle may be cited as the Maryland Anatomical Gift Act. (An. Code 1957, art. 43, § 149B; 1974, ch. 11, § 2; 1976, ch. 273, § 1.)

Effect of amendment. — The 1976 amendment, effective July 1, 1976, added "Maryland."

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